(b) periodically determining levels of a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues, or bodily fluid from said patient; and

(c) comparing the periodically determined levels of the CSG with levels of the CSG measured in cells, tissues, or bodily fluid of a normal human control, wherein an increase in any one of the periodically determined levels of the CSG in the patient versus the normal human control is associated with a cancer that is progressing in stage and a decrease is associated with a cancer that is regressing in stage or in remission.

REMARKS

Claims 1-12 are pending in the instant application. Claims 6 and 8-12 have been withdrawn from consideration by the Examiner. Claims 1-5 and 7 have been rejected. Claims 6-12 have been canceled. Claims 1-5 have been amended. No new matter has been added by these amendments to the claims. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Restriction Requirement

The Restriction Requirement grouping the claims into Group I, claims 1-5 and 7, Group II, claims 6 and 7, Group III, claim 8, Group IV, claims 9 and 10, Group V, claim 11, and Group VI, claim 12, wherein Applicants elected Group I, with traverse, was deemed proper and made final. Applicants have canceled claims 6 and 8-12 without prejudice with Applicants reserving the right to file continuing applications on the canceled subject matter.

II. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claims 1-5 and 7 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner suggests that the recitation of the term "CSG" is vague and indefinite. Applicants have amended the claims to specify that CSG is a protein expressed by a colon specific gene and comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, of the present invention. Withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 102(b)

Claims 1 and 2 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,733,748. The Examiner suggests that this patent discloses methods for diagnosing the presence of colon cancer and metastases of colon cancer in a patient that are based on determination of levels of CSG in samples from the patient's bodily fluids. Applicants respectfully traverse this rejection.

Applicants have amended claims 1 and 2 to recite that the CSG of the present invention is a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, as taught throughout the specification as filed, but in particular at pages 6-7.

U.S. Patent No. 5,733,748 discloses several polynucleotides and polypeptides relating to colon specific genes. The patent discusses 13 such CSG genes. Although the patent mentions that levels of expression of these CSG genes may be used as a diagnostic aid in colon cancer, the sequences taught for these CSG's are not the same as SEQ ID NO: 1 of the present invention. In particular, Figures 8 and 9 of the patent show the sequence of the only two CSG's that the patent discloses in full. Neither of these

two sequences is the same as the sequence of the present invention. Therefore, nowhere does this prior art reference teach or suggest screening for the presence of levels of the protein expressed by the gene of the present invention. In order to anticipate an invention the prior art reference must teach each and every element of the claimed invention (MPEP 2131). Accordingly, this reference cannot anticipate the claims as amended and withdrawal of the rejection is respectfully requested.

Claims 1 and 2 have been rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/39419. The Examiner suggests that this patent application discloses methods for diagnosing the presence of colon cancer and metastases of colon cancer in a patient where the levels of CSG in samples from the patients cells or bodily fluids are indicative of colon cancer. Applicants respectfully traverse this rejection.

As discussed *supra*, Applicants have amended claims 1 and 2 to specify detection of levels of a CSG comprising a polynucleotide sequence of its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby. The patent application cited (WO 96/39419) discusses 13 CSG genes. Although the patent mentions that the levels of expression of these CSG genes may be used as a diagnostic aid in colon cancer, the

sequences taught for these CSG's are not the same as SEQ ID NO: 1. In particular, Figures 8 and 9 of the prior art patent show the sequence of the only two CSG's that the patent discloses in full. Neither of these two sequences is the same as the sequence of the present invention. Therefore, nowhere does this prior art reference teach or suggest screening for the presence of levels of the protein expressed by the gene of the present invention. In order to anticipate an invention the prior art reference must teach each and every element of the claimed invention (MPEP 2131). Accordingly, this reference cannot anticipate the claims as amended and withdrawal of the rejection is respectfully requested.

IV. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1-5 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,733,748 and WO 96/39419. The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill to implement methods of staging and monitoring colon cancer in a patient for changes in staging as well as for the onset of metastasis considering that the methods of diagnosing colon cancer and metastases are well established and that these prior art patents teach that CSG levels are related to colon cancer. Applicants respectfully traverse this rejection.

As discussed in detail *supra* in Section II, these two prior art references fail to teach the CSG of the present invention.

To establish a *prima facie* case of obviousness toward the claimed invention, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. See MPEP § 2143. The combination of references cited by the Examiner clearly fails to meet all these criteria with respect to the claims. Specifically, the references fail to teach or suggest all of the claim limitations, namely a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby. Accordingly, this combination of prior art does not render obvious the instant claimed invention. Withdrawal of this rejection is therefore respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: **July 5, 2001**

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 6-12 have been canceled without prejudice.

Claims 1-5 have been amended as follows:

1. (amended) A method for diagnosing the presence of colon cancer in a patient comprising:

(a) determining levels of a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues or bodily fluids in a patient; and

(b) comparing the determined levels of the CSG with levels of the CSG in cells, tissues or bodily fluids measured in ~~from~~ a normal human control, wherein a change in determined levels of the CSG in said patient versus levels of the CSG measured in a normal human control is associated with the presence of colon cancer.

2. (amended) A method of diagnosing metastases of colon cancer in a patient comprising:

(a) identifying a patient having colon cancer that is not known to have metastasized;

(b) determining levels of a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, ~~levels~~ in a first sample of cells, tissues or bodily fluid from said patient; and

(c) comparing the determined levels of the CSG ~~levels~~ with levels of the CSG measured in a second sample of cells, tissues or bodily fluid ~~of~~ from a normal human control, wherein an increase in determined levels of the CSG ~~levels~~ in the ~~patient versus the normal human control~~ first sample as compared to the second sample is associated with a cancer ~~which~~ that has metastasized.

3. (amended) A method of staging colon cancer in a patient having colon cancer comprising:

(a) identifying a patient having colon cancer;

(b) determining levels of a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide

encoded thereby, ~~levels~~ in a first sample of cells, tissues or bodily fluid from said patient; and

(c) comparing the determined levels of the CSG ~~levels~~ with levels of the CSG measured in a second sample of cells, tissues or bodily fluid ~~of~~ from a normal human control, wherein an increase in the determined levels of the CSG ~~levels~~ in ~~said~~ the ~~patient versus normal human control~~ first sample as compared to the second sample is associated with a cancer ~~which~~ that is progressing and a decrease in the determined levels of the CSG ~~levels~~ in the first sample as compared to the second sample is associated with a cancer ~~which~~ that is regressing or in remission.

4. (amended) A method of monitoring colon cancer in a patient for the onset of metastasis comprising:

(a) identifying a patient having colon cancer that is not known to have metastasized;

(b) periodically determining levels of a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in samples of cells, tissues, or bodily fluid from said patient; and

(c) comparing the periodically determined levels of the CSG ~~levels~~ with levels of the CSG measured in cells, tissues or bodily fluid of a normal human control, wherein an increase in any one of the periodically determined levels of the CSG ~~levels~~ in the patient versus the normal human control is associated with a cancer ~~which~~ that has metastasized.

5. (amended) A method of monitoring a change in stage of colon cancer in a patient comprising:

(a) identifying a patient having colon cancer;

(b) periodically determining levels of a CSG comprising a polynucleotide sequence or its complement capable of hybridizing under stringent conditions with SEQ ID NO: 1, or a polypeptide encoded thereby, in cells, tissues, or bodily fluid from said patient; and

(c) comparing the periodically determined levels of the CSG ~~levels~~ with levels of the CSG measured in cells, tissues, or bodily fluid of a normal human control, wherein an increase in any one of the periodically determined levels of the CSG ~~levels~~ in the patient versus the normal human control is associated with a cancer ~~which~~ that is progressing in stage and a decrease is associated with a cancer ~~which~~ that is regressing in stage or in remission.